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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,271	09/19/2006	Arturo Jimenez-Bayardo	PORF4.002APC	8047

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EXAMINER	
KASTURI, SRIRAM	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
09/15/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/564,271	JIMENEZ-BAYARDO ET AL.	
	Examiner	Art Unit	
	SRIRAM KASTURI	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-9 are pending.

Claim Rejections - 35 USC § 112

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2 recite the term 'pouring of 1000 ml of ethyl alcohol' into a 'precipitate recipient'. It is not clear whether the precipitate recipient is a container or something else.

Claims 5 and 6 use carrier solution Sophisen®. Specification does not contain the composition of Sophisen®. The use of the trademark Sophisen® has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant states that though Sophisen® is an ideal carrier solution other suitable carrier solutions that fulfill similar characteristics can also be used in the formulation. (Specification, page 5, lines 3-8).

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicants claim a preparation method of aqueous ophthalmic meloxicam solution and its composition. Their method comprises dissolving meloxicam in ethanol either alone or in combination with methyliden (methylidinoglycerol) adding polysorbate 80, N sodium hydroxide and carrier solution while shaking.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over teachings of Folger et al (US Pub no. 2003/0119825).

Folger et al teach highly stable meloxicam solutions containing pharmacologically acceptable sodium meloxicam salt with one or more suitable excipients they also teach preparation method of their formulation (Page 3, Claims 1 and 2). Their teachings include low concentration of meloxicam 0.5% for eye drop solutions (Page 1, paragraph 0004, lines 1 and 2).

Their method of preparation is described in detail (Page 3, paragraph 0037, 0038) and in example (Page 3, paragraph 0035). 4 g of meloxicam is dissolved in aqueous meglumine solution (1.4g/50 ml) at 90^{o}C and other excipients are added one after other. Their teachings include use of sodium salt of meloxicam or meglumine (Page 2, paragraph 0014, lines 1 and 2) in their formulation. So alternatively 4 g of meloxicam is dissolved in 15.6 g ethanol as density of ethanol is 0.789 g/cm^{3} liquid, 15.6 g equals to about 12.48 ml. Other excipients like 15.0g of Macrogel 300 (polyethylene glycol) and 5.0g of Poloxamer 188 (polyoxyethylene-polyoxypropylene copolymer) as a carrier and 0.5g of glycine are added one after the other. The pH is adjusted to 8.8 using 1M hydrochloric acid and 1M sodium hydroxide solution, and the volume is made up to 100 ml using water. The concentration of solubilisers like glycine can be up to 200 mg/ml (Page 2, paragraph 0017, lines 1 and 2). As these are being added sequentially, it would be obvious to one of ordinary skill in the art to add while shaking are stirring the mixture to obtain homogenous formulation with pH 8.8.

Applicant claims a method for preparing final volume of 100 L of meloxicam solution, where as Folger et al's method is for preparing 100 ml of meloxicam formulation , thus there is a 1000 fold difference in the final volumes. In Claim 2

applicant is mixing ethyl alcohol with meloxicam, sodium hydroxide and polysorbate 80. Thus their formulation can be prepared with or without methyliden. Folger et al teach use of polyethyleneglycol, polysorbate, glycerol as solubilisers. Methyliden or Methylidinoglycerol (Specification page 4, line 6) is a glycerol derivative thus glycerol of Folger et al formulation can be replaced by methyliden. Additionally applicant also includes glycerin (glycerol) in addition to methyldinoglycerol as one of the viscosity increasing agents (Specification, page 2 , line 30) indicating that one can be replaced for the other.

Folger et al's formulation contains meloxicam, meloxicam salt, solubilisers polyethyleneglycol, polysorbate, glycerol, sorbital, mannitol (Page 1, paragraph 0011, lines 1, 7 and 8). Polysorbates include polysorbate 20-80 also known to one of ordinary skill in the art as Tween 20-80. Thus Folger et al's teachings include meloxicam, polyoxyethylene-polyoxypropylene copolymer used as a solubiliser (Page 1, paragraph 0011, lines 3-4) can be used as a carrier also, as applicant indicates that any carrier solution with similar characteristics can be used instead of Sophisen® (Specification, page 5, lines 5-8). Folger et al's composition also contains glycerol (viscosity increasing agent), polysorbate (surface active, moisturizing agent), mannitol (osmolarity regulating agent) and benzoic acid as preservative (Page 2, paragraph 0019, lines 1 and 2). Folger et al's teachings include use of disodium EDTA as an additional excipient (Page 2, paragraph 0014, line 12). Disodium EDTA also known as disodium edetate is an antioxidant agent (Specification, page 3, line 5).

They also teach a buffer substance for achieving the optimal pH range between 8.0 to 10 (Page 3, claim 10).

Thus Folger et al's meloxicam formulation contains ethanol, polyoxyethylene-polyoxypropylene copolymer as a carrier, glycerol (viscosity increasing agent), polysorbate (surface active, moisturizing agent), mannitol (osmolarity regulating agent) and benzoic acid as a preservative, disodium EDTA as an antioxidant agent, and a buffer substance for achieving the optimal pH range as described above. This composition at lower meloxicam concentraion of 0.5% can be used as ophthalmic formulation for treating ocular affections.

Though Folger et al's method of meloxicam formulation preparation is in smaller scale compared to applicant's method, Folger et al's method can be used by scaling up the individual components for preparing larger quantities as they follow similar steps as used by applicant, and same formulation can be used as ophthalmic formulation at lower meloxicam concentraions. Thus there is motivation to one of ordinary skill in the art to make necessary changes to prepare a large scale ophthalmic formulation of Folger et al for treating ocular affections. Additionally it would be obvious to one of ordinary skill in the art to modify the concentration of individual components to obtain desired effects.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over teachings of Miyake et al (US6,495,603 B1) and Folger et al. (US Pub no. 2003/0119825).

Miyake et al teach anti-inflammatory aqueous eye drop comprising meloxicam (Abstract) and its method of preparation (Col.4, example 3, lines 5-20). Their teachings include use of meloxicam at 0.1% to 1% for treating inflammatory disease (Col.3, lines 5-7). Their method includes adding meloxicam, Tween-80 (Polysorbate-80) surface active and moisturizing agent, methyl cellulose (viscosity increasing agent) at 0.5 g each respectively, boric acid (buffering system) at 0.1 g, EDTA and benzalkonium chloride (preservative) at 0.005 g each to dissolve these components in water. It would be obvious to one of ordinary skill in the art to add these components in a sequential order while stirring are shaking to obtain homogenous formulation while adjusting pH value of the resulting solution to 7.2 by the addition of 0.1N HCl or 0.1N NaOH and purified water was further added to the solution to give a total volume of 100 ml (Col.4, example 3, lines 5-23).

Miyake et al's meloxicam aqueous eye drop formulation method lack ethanol and a carrier.

Folger et al teach highly stable meloxicam solutions. Their teachings include use of low concentration of meloxicam for eye drops. Folger et al's meloxicam formulation preparation method contains ethanol, polyoxyethylene-polyoxypropylene copolymer as a carrier in addition to other necessary components as described above.

It would be obvious to one of ordinary skill in the art to add ethanol and polyoxyethylene-polyoxypropylene copolymer as a carrier in Miyake et al eye drop method of formulation preparation as taught by Folger et al as a solubiliser, and both teach eye drop formulation preparation methods as described above. In addition there is

atleast an expectation of additive effect in solubilisation of meloxicam by addition of an additional solubiliser.

Though Miyake et al's method of meloxicam formulation preparation is in smaller scale compared to applicant's method, Miyake et al's method of preparation can be used by scaling up the individual components for preparing larger quantities as they follow similar steps as used by applicant. Thus there is motivation to one of ordinary skill in the art to make necessary changes to prepare a large scale ophthalmic formulation of Miyake et al for treating ocular affections. Additionally it would be obvious to one of ordinary skill in the art to modify the concentration of individual components to obtain desired effects.

There is reasonable expectation success in a preparation method of aqueous meloxicam formulation for treating ocular affections.

Conclusion

Claims 1-9 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SRIRAM KASTURI whose telephone number is (571)270-5263. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sriram Kasturi/
Examiner

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612